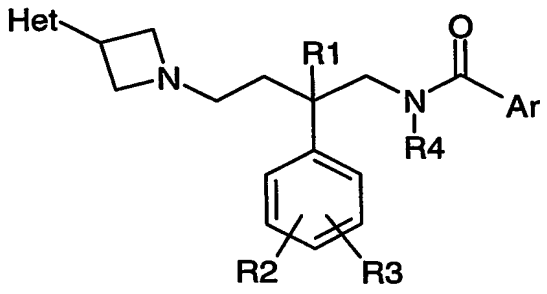
Claims

1. A compound of the general formula (I)



(I)

wherein

Het is an optionally substituted 4-, 5-, 6- or 7-membered heterocyclic ring having at least one nitrogen atom;

R1 is hydrogen, hydroxy, C_1-C_4 alkyl, C_3-C_4 cycloalkyl, C_2-C_4 alkenyl or C_2-C_4 alkynyl;

R2 and R3 is each and independently selected from hydrogen, C_1-C_4 alkyl, C_3-C_4 cycloalkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 alkoxy, halogen and cyano, provided that R2 and R3 may not both be hydrogen;

R4 is C_1-C_4 alkyl, C_3-C_4 cycloalkyl, C_2-C_4 alkenyl or C_2-C_4 alkynyl;

Ar is an optionally substituted aromatic ring system selected from pyridinyl; 1-naphthyl; 5,6,7,8-tetrahydro-1-naphthyl; quinolinyl; 2,3-dihydro-1,4-benzodioxinyl; 1,3-benzodioxolyl; 5,6,7,8-tetrahydroquinolinyl; 5,6,7,8-tetrahydroisoquinolinyl; 5,6,7,8-tetrahydroquinazolin-4-yl; 1-benzo[b]thiophen-7-yl; 1-benzo[b]thiophen-4-yl; 1-benzo[b]thiophen-3-yl; isoquinolinyl; quinazolinyl; and indan-4-yl; or Ar is substituted phenyl;

or an enantiomer thereof or any salt thereof.

2. A compound according to claim 1 wherein

Het is an optionally substituted 4, 5, 6 or 7-membered heterocyclic ring containing one or more nitrogen atoms;

R1 is hydrogen, hydroxy or C_1-C_4 alkyl;

R2 and R3 are independently hydrogen, C_1-C_4 alkoxy, halogen, CF_3 or cyano, provided that both are not hydrogen;

R4 is C_1-C_4 alkyl;

Ar is an optionally substituted aromatic ring system selected from pyridinyl; 1-naphthyl; 5,6,7,8-tetrahydro-1-naphthyl; quinolinyl; 2,3-dihydro-1,4-benzodioxinyl; 1,3-benzodioxolyl; 5,6,7,8-tetrahydroquinolinyl; 5,6,7,8-tetrahydroisoquinolinyl; 5,6,7,8-tetrahydroquinazolin-4-yl; 1-benzo[b]thiophen-7-yl; 1-benzo[b]thiophen-4-yl; 1-benzo[b]thiophen-3-yl; isoquinolinyl; quinazolinyl; and indan-4-yl; or Ar is substituted phenyl;

or an enantiomer thereof or any salt thereof.

3. A compound according to claim 1 or 2, wherein Ar is an optionally substituted aromatic ring system selected from 1-naphthyl; 5,6,7,8-tetrahydro-1-naphthyl; quinolinyl; 2,3-dihydro-1,4-benzodioxinyl; 1,3-benzodioxolyl; 5,6,7,8-tetrahydroquinolinyl; 5,6,7,8-tetrahydroisoquinolinyl; 5,6,7,8-tetrahydroquinazolin-4-yl; 1-benzo[b]thiophen-7-yl; 1-benzo[b]thiophen-4-yl; 1-benzo[b]thiophen-3-yl; isoquinolinyl; quinazolinyl; and indan-4-yl.

4. A compound according to claim 3, wherein Ar is substituted by one or more groups independently selected from cyano, halogen, C_1-C_4 alkyl, C_3-C_4 cycloalkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 alkoxy, nitro, trifluoromethoxy, difluoromethoxy, trifluoromethyl,

C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylthio, trifluoromethylsulfonyloxy, C_1-C_4 alkyl sulfonyl or C_1-C_4 acyl.

5. A compound according to claim 1 or 2, wherein Ar is substituted phenyl.

6. A compound according to claim 5, wherein Ar is phenyl substituted in its 3- and 5-position by groups independently selected from halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, cyano and nitro.

7. A compound according to claim 6, wherein Ar is also substituted in its 2- and/or 4-position by a group independently selected from halogen, C_1-C_4 alkyl and C_1-C_4 alkoxy.

8. A compound according to any one of claims 1-7, wherein the heterocyclic ring Het is connected to the rest of the molecule at one of the nitrogen atoms of the ring.

9. A compound according to any one of claims 1-8, whererin the heterocyclic ring Het is selected from the group of optionally substituted piperidino; optionally substituted azepano; optionally substituted pyrrolidino; optionally substituted morpholino; optionally substituted oxazepano; optionally substituted thiomorpholino; optionally substituted thiazepano; and optionally substituted piperazino.

10. A compound according to claim 9, wherein the heterocyclic ring Het is piperidino optionally substituted with hydroxy, hydroxyalkyl, oxo, methylthio, methylsulfinyl, methylsulfonyl, cyano, 1,3-dioxolan-2-yl, C_1-C_4 alkoxy, amino optionally mono or disubstituted with C_1-C_4 alkyl, C_3-C_4 cycloalkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, acylamino optionally N-substituted with C_1-C_4 alkyl, C_3-C_4 cycloalkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, (C_1-C_4 alkylsulfonyl)amino optionally N-substituted by C_1-C_4 alkyl, C_3-C_4 cycloalkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, one or two fluoro atoms or disubstituted by C_1-C_4 alkyl and hydroxy.

11. A compound according to claim 9, wherein the heterocyclic ring Het is pyrrolidino optionally substituted at its three position by fluoro, hydroxy or oxo.

12. A compound according to claim 9, wherein the heterocyclic ring Het is morpholino or thiomorpholino optionally substituted at its sulfur atom by one or two oxygen.

13. A compound according to claim 9, characterized in that the heterocyclic ring Het is piperazino optionally substituted at the 4-nitrogen atom by C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_4 cycloalkyl, C_1-C_4 alkyl sulfonyl or C_1-C_4 acyl.

14. A compound according to claim any one of claims 1-13, wherein R1 is hydrogen.

15. A compound according to any one of claims 1-14, wherein R2 and R3 are both chloro.

16. A compound according to claim 15, wherein R2 and R3 are both chloro and attached in the three and four position of the phenyl ring.

17. A compound according to any one of claims 1-14, wherein R2 is fluoro and R3 is hydrogen.

18. A compound according to claim 17, wherein R2 is fluoro attached in the four position and R3 is hydrogen.

19. A compound according to any one of claims 1-18, wherein R4 is methyl.

20. A compound according to claim 1, wherein

Het is thiomorpholino, morpholino or oxidothiomorpholino;

R1 is H;

R2 is fluoro;

R3 is hydrogen;

Ar is 3-cyano-5,6,7,8-tetrahydro-1-naphthyl.

21. A compound according to any one of claims 1-20 wherein the compound is the S-enantiomer.

22. A compound according to claim 1 selected from

3,5-Dichloro-*N*-[(2*S*)-2-(3,4-dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methylbenzamide;

3,5-Dibromo-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methylbenzamide;

N-[(2S)-2-(3,4-Dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-3,5-difluoro-*N*-methylbenzamide;

N-[(2*S*)-2-(3,4-Dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

5-Cyano-*N*-[(2*S*)-2-(3,4-dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-1-benzothiophene-7-carboxamide;

3-Cyano-*N*-[(2S)-2-(3,4-dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methylbenzamide;

3-Cyano-*N*-[(2*S*)-2-(3,4-dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

2-Cyano-*N*-[(2*S*)-2-(3,4-dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methylquinoline-4-carboxamide;

3-Cyano-*N*-[2-(4-fluorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

N-[2-(4-Fluorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

7-Chloro-*N*-[(2*S*)-2-(3,4-dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-2,3-dihydro-1,4-benzodioxine-5-carboxamide;

N-{(2*S*)-2-(3,4-Dichlorophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-2-methoxy-*N*-methylquinoline-4-carboxamide;

3-Fluoro-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-5-(trifluoromethyl)benzamide;

3-Cyano-*N*-{2-(4-fluorophenyl)-4-[3-(4-hydroxypiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

N-[4-[3-(1,4-Dioxa-8-azaspiro[4.5]dec-8-yl)azetidin-1-yl]-2-(4-fluorophenyl)butyl]-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

N-{(2*S*)-2-(3,4-Dichlorophenyl)-4-[3-(4-fluoropiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

N-{(2*S*)-2-(3,4-Dichlorophenyl)-4-[3-(4-hydroxypiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

3-Cyano-*N*-{(2S)-2-(3,4-dichlorophenyl)-4-[3-(3-hydroxypyrrolidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-1-naphthamide;

N-{(2*S*)-2-(4-Fluorophenyl)-4-[3-(4-fluoropiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

3-Cyano-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

N-{(2*S*)-2-(4-fluorophenyl)-4-[3-(4-hydroxypiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

3,5-Dichloro-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methylbenzamide;

3-Cyano-*N*-[(2*S*)-2-(3,4-dichlorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-1-naphthamide;

3-Cyano-*N*-[(2*S*)-2-(3,4-dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-1-naphthamide;

3-Cyano-*N*-{(2S)-2-(3,4-dichlorophenyl)-4-[3-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)azetidin-1-yl]butyl}-*N*-methyl-1-naphthamide;

3-Cyano-*N*-{(2*S*)-2-(3,4-dichlorophenyl)-4-[3-(4-hydroxypiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-1-naphthamide;

3-Cyano-*N*-[2-(4-fluorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-1-naphthamide;

3-Cyano-*N*-[2-(4-cyanophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-1-naphthamide;

3-Cyano-*N*-{(2*S*)-2-(3,4-dichlorophenyl)-4-[3-(1,1-dioxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-*N*-methyl-1-naphthamide;

3-Cyano-*N*-{(2*S*)-2-(4-fluorophenyl)-4-[3-(4-hydroxypiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

3-Cyano-*N*-ethyl-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

3-Cyano-*N*-[(2*S*)-4-[3-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)azetidin-1-yl]-2-(4-fluorophenyl)butyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

3-cyano-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-1-naphthamide;

3-Cyano-*N*-{(2*S*)-2-(4-fluorophenyl)-4-[3-(1,4-oxazepan-4-yl)azetidin-1-yl]butyl}-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

3-Fluoro-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

3,5-Dibromo-*N*-{(2*S*)-2-(4-fluorophenyl)-4-[3-(4-hydroxypiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methylbenzamide;

3-Bromo-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-5-iodo-*N*-methylbenzamide;

3-Cyano-*N*-[2-(4-fluoro-2-methylphenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

6-Cyano-*N*-[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-*N*-methylindane-4-carboxamide;

3-Cyano-*N*-{(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-*N*-methyl-1-naphthamide;

3-Cyano-*N*-{2-(4-cyanophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-*N*-methyl-1-naphthamide;

3,5-Dichloro-*N*-{(2*S*)-2-(3,4-dichlorophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-*N*-methylbenzamide;

N-[(2S)-2-(3,4-Dichlorophenyl)-4-(3-oxidothiomorpholin-4-ylazetidin-1-yl)butyl]-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

3-Cyano-*N*-{(2*S*)-2-(3,4-dichlorophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

3-Cyano-*N*-{2-(4-fluorophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-*N*-methyl-1-naphthamide;

3-cyano-*N*-{2-(4-fluorophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

N-{2-(4-Fluorophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl}-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

3-Cyano-N-{(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-oxopiperidin-1-yl)azetidin-1-yl]butyl}-N-methyl-1-naphthamide;

N-{2-(4-fluorophenyl)-4-[3-(4-oxopiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-3,5-bis(trifluoromethyl)benzamide;

3-Cyano-N-{(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-fluoropiperidin-1-yl)azetidin-1-yl]butyl}-N-methyl-1-naphthamide;

3-Cyano-*N*-{2-(4-fluorophenyl)-4-[3-(4-fluoropiperidin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

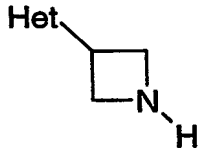
3-Cyano-*N*-{(2*S*)-2-(3,4-dichlorophenyl)-4-[3-(4-methylpiperazin-1-yl)azetidin-1-yl]butyl}-*N*-methyl-1-naphthamide;

N-[(2*S*)-4-[3-(4-Acetylpiperazin-1-yl)azetidin-1-yl]-2-(3,4-dichlorophenyl)butyl]-3-cyano-*N*-methyl-1-naphthamide;

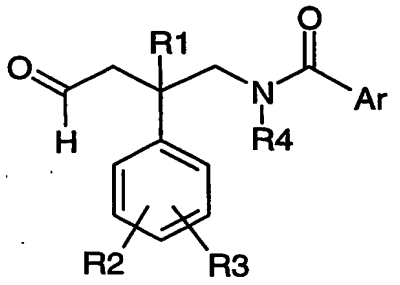
3-Cyano-*N*-[(2*S*)-4-[3-(4-cyanopiperidin-1-yl)azetidin-1-yl]-2-(3,4-dichlorophenyl)butyl]-*N*-methyl-1-naphthamide;

or an enantiomer thereof or any salt thereof.

23. A process for preparing a compound according to any one of claims 1-22, which process comprises a) reacting a compound of the formula (III) with a compound of the formula (IV):



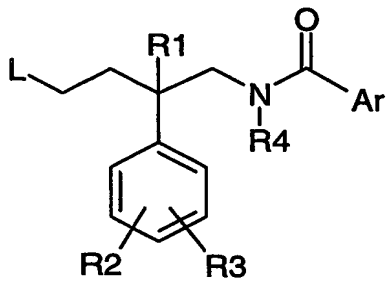
(III)



(IV)

wherein R1-R4, Het, and Ar are as hereinbefore defined; and the conditions are such that reductive alkylation of the compounds of the formulae (III) forms an N-C bond between the nitrogen atom of the azetidine group of the compounds of formulae (III) and the carbon atom of the aldehyde group of the compounds of formulae (IV); or

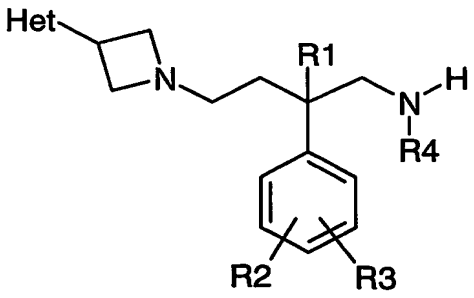
b) reacting a compound of the formula (III) with a compound of the formula (V):



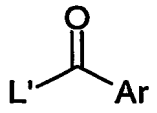
(V)

wherein R1-R4, Het, and Ar are as hereinbefore defined; and L is a group such that alkylation of the compounds of the formulae (III) forms an N-C bond between the nitrogen atom of the azetidine group of the compounds of formulae (III) and the carbon atom of the compounds of formulae (V) that is adjacent to the L group; or

c) reacting a compound of the formula (VI) with a compound of the formula (VII):



(VI)



(VII)

wherein R1-R4, Het and Ar are as hereinbefore defined; and L' is a leaving group;

wherein any other functional group is protected, if necessary, and:

i) removing any protecting groups;

ii) optionally oxidizing any oxidizeable atoms;

iii) optionally forming a pharmaceutically acceptable salt.

24. A compound selected from

[(2*S*)-2-(3,4-dichlorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]methylamine;

[(2*S*)-2-(3,4-dichlorophenyl)-4-[3-(1-oxidothiomorpholin-4-yl)azetidin-1-yl]butyl]methylamine;

[2-(4-fluorophenyl)-4-(3-thiomorpholin-4-ylazetidin-1-yl)butyl]methylamine;

[(2*S*)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]methylamine;

1-{1-[3-(4-fluorophenyl)-4-(methylamino)butyl]azetidin-3-yl}piperidin-4-ol;

[4-[3-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)azetidin-1-yl]-2-(4-fluorophenyl)butyl]methylamine;

{(2*S*)-2-(3,4-dichlorophenyl)-4-[3-(4-fluoropiperidin-1-yl)azetidin-1-yl]butyl}methylamine;

1-{1-[(3*S*)-3-(3,4-dichlorophenyl)-4-(methylamino)butyl]azetidin-3-yl}piperidin-4-ol;

1-[(3*S*)-4-[(3-cyano-1-naphthoyl)(methyl)amino]-3-(3,4-dichlorophenyl)butyl]azetidin-3-yl;

3-cyano-*N*-[2-(4-fluorophenyl)-4-oxobutyl]-*N*-methyl-1-naphthamide;

3-cyano-*N*-[2-(4-cyanophenyl)-4-oxobutyl]-*N*-methyl-1-naphthamide;

3-cyano-*N*-[(2*S*)-2-(4-fluorophenyl)-4-oxobutyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

3,5-dichloro-*N*-[(2*S*)-2-(4-fluorophenyl)-4-oxobutyl]-*N*-methylbenzamide;

3-cyano-*N*-ethyl-*N*-[(2*S*)-2-(4-fluorophenyl)-4-oxobutyl]-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

3-cyano-*N*-[(2*S*)-2-(4-fluorophenyl)-4-oxobutyl]-*N*-methyl-1-naphthamide;

3,5-dibromo-*N*-[(2*S*)-2-(4-fluorophenyl)-4-oxobutyl]-*N*-methylbenzamide;

3-bromo-*N*-[(2*S*)-2-(4-fluorophenyl)-4-oxobutyl]-5-iodo-*N*-methylbenzamide;

3-cyano-*N*-[2-(4-fluoro-2-methylphenyl)-4-oxobutyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

6-cyano-*N*-[(2*S*)-2-(4-fluorophenyl)-4-oxobutyl]-*N*-methylindane-4-carboxamide;

3-fluoro-*N*-[(2*S*)-2-(4-fluorophenyl)-4-oxobutyl]-*N*-methyl-5,6,7,8-tetrahydronaphthalene-1-carboxamide;

or an enantiomer thereof or any salt thereof.

25. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound of any one of claims 1-22 as a single enantiomer, a racemate or a mixture thereof in the form of a free base or a pharmaceutically acceptable salt or solvate thereof optionally in association with diluents, excipients or inert carriers.

26. Use of a compound according to any one of claims 1-22, as a single enantiomer, a racemate or a mixture thereof in the form of a free base or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for use in the prevention or treatment of respiratory, cardiovascular, neuro, pain, oncology, inflammatory and/or gastrointestinal disorders.

27. The use according to claim 26 in the manufacture of a medicament for use in the prevention or treatment of asthma, allergic rhinitis, pulmonary, cough, cold, inflammation, chronic obstructive pulmonary disease, airway reactivity, urticaria, hypertension, rheumatoid arthritis, edema, angiogenesis, pain, migraine, tension headache, psychoses, depression, anxiety, Alzheimer's disease, schizophrenia, Huntington's disease, bladder hypermotility, urinary incontinence, eating disorder, manic depression, substance dependence, movement disorder, cognitive disorder, obesity, stress disorders, micturition disorders, mania, hypomania and aggression, bipolar disorder, cancer, carcinoma, gastrointestinal hypermotility, gastric asthma, Crohn's disease, gastric emptying disorders, ulcerative colitis, irritable bowel syndrome, inflammatory bowel disease, emesis, gastric motility disorders or gastro-esophageal reflux disease (GERD).

28. A method of preventing or treating respiratory, cardiovascular, neuro, pain, oncology and/or gastrointestinal disorders comprising administering an effective amount of a compound according to any one of claims 1-22 as a single enantiomer, a racemate or a mixture thereof in the form of a free base or a pharmaceutically acceptable salt or solvate thereof.

29. The method according to claim 28 wherein gastrointestinal hypermotility, gastric asthma, Crohn's disease, gastric emptying disorders, ulcerative colitis, irritable bowel syndrome, inflammatory bowel disease, emesis, gastric motility disorders or gastro-esophageal reflux disease (GERD) is prevented or treated.

30. A compound as defined in any one of claims 1-22 for use in therapy.

31. A compound as defined in claim 30 for use in the prevention or treatment of respiratory, cardiovascular, neuro, pain, oncology, inflammatory and/or gastrointestinal disorders.

32. A compound as defined in claim 31 for use in the prevention or treatment of asthma, allergic rhinitis, pulmonary, cough, cold, inflammation, chronic obstructive pulmonary disease, airway reactivity, urticaria, hypertension, rheumatoid arthritis, oedema, angiogenesis, pain, migraine, tension headache, psychoses, depression, anxiety, Alzheimer's disease, schizophrenia, Huntington's disease, bladder hypermotility, urinary incontinence, eating disorder, manic depression, substance dependence, movement disorder, cognitive disorder, obesity, stress disorders, micturition disorders, mania, hypomania and aggression, bipolar disorder, cancer, carcinoma, fibromyalgia, non cardiac chest pain, gastrointestinal hypermotility, gastric asthma, Crohn's disease, gastric emptying disorders, ulcerative colitis, irritable bowel syndrome, inflammatory bowel disease, emesis, gastric motility disorders or gastro-esophageal reflux disease (GERD).